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Analogous enzymes: independent inventions in enzyme evolution.

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It is known that the same reaction may be catalyzed by structurally unrelated enzymes. We performed a systematic search for such analogous (as opposed to homologous) enzymes by evaluating sequence conservation among enzymes with the same enzyme classification (EC) number using sensitive, iterative sequence database search methods. Enzymes without detectable sequence similarity to each other were found for 105 EC numbers (a total of 243 distinct proteins). In 34 cases, independent evolutionary origin of the suspected analogous enzymes was corroborated by showing that they possess different structural folds. Analogous enzymes were found in each class of enzymes, but their overall distribution on the map of biochemical pathways is patchy, suggesting multiple events of gene transfer and selective loss in evolution, rather than acquisition of entire pathways catalyzed by a set of unrelated enzymes. Recruitment of enzymes that catalyze a similar but distinct reaction seems to be a major scenario for the evolution of analogous enzymes, which should be taken into account for functional annotation of genomes. For many analogous enzymes, the bacterial form of the enzyme is different from the eukaryotic one; such enzymes may be promising targets for the development of new antibacterial drugs.

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